

CLAIMS

We claim:

1. A transgenic non-human mammal whose genome is heterozygous for a mutation engineered into the Erk5 gene, wherein in a homozygous state said mutation results in a functionally deficient Erk5 gene and embryonic death characterized by a lack of vasculogenesis and angiogenesis in said homozygous embryo.

2. A cell isolated from the transgenic non-human mammal according to claim 1, wherein said cell is isolated from said mammal at the embryonic stage or at the post partum stage.

3. A transgenic non-human mammalian embryo whose genome is homozygous for a mutation engineered into the Erk5 gene, wherein said mutation results in a functionally deficient Erk5 gene and embryonic death characterized by a lack of vasculogenesis and angiogenesis in said homozygous embryo.

4. A cell isolated from the transgenic non-human mammalian embryo according to claim 3.

5. An isolated cell heterozygous for a mutation engineered into the Erk5 gene, wherein said mutation results in a functionally deficient Erk5 gene, wherein said cell is produced by introducing a mutated Erk5 gene into a cell containing a functional Erk5 gene.

6. A chimeric non-human mammal which comprises cells that are heterozygous for a mutation engineered into

the Erk5 gene, wherein, in a homozygous state, said mutation results in a functionally deficient Erk5 gene and wherein a mammalian embryo whose genome is homozygous for said mutation is characterized by a lack of vasculogenesis and angiogenesis and a failure to survive to birth.

7. A cell isolated from the chimeric non-human mammal according to claim 6, wherein said cell is heterozygous for a defect engineered into the Erk5 gene.

8. The transgenic mammal according to claim 1, wherein said mammal is a mouse.

9. The transgenic mammalian embryo according to claim 3, wherein said embryo is a mouse embryo.

10. The chimeric mammal according to claim 6, wherein said mammal is a mouse.

11. The isolated cell according to any one of claims 2, 4, 5, or 7, wherein said cell is a mouse cell.

12. The isolated cell according to claim 11, wherein said cell is an embryonic stem cell.

13. A method of treating or preventing a condition characterized by angiogenesis in an animal comprising the step of administering to said animal a pharmaceutically acceptable composition comprising a
5 molecule which inhibits any of the transcription of an Erk5 gene, the translation of an Erk5 mRNA or the

activity of an Erk5 protein; and a pharmaceutically acceptable carrier.

14. The method according to claim 13, wherein
5 said molecule is selected a monoclonal or polyclonal antibody specific for Erk5, an oligonucleotide that specifically hybridizes to Erk5 DNA so as to prevent transcription of functional Erk5 mRNA, an oligonucleotide that specifically hybridizes to Erk5 mRNA to as to
10 prevent expression of Erk5, a ribozyme that specifically cleaves Erk5 mRNA, or a small molecule inhibitor or antagonist of Erk5 protein.

15. The method according to claim 13, wherein
15 said condition is selected from brain cancer, genitourinary tract cancer, lymphatic system cancer, stomach cancer, cancer of the larynx, lung cancer, pancreatic cancer, breast cancer, Kaposi's sarcoma, retinoblastoma, neuroblastoma, Wilm's tumor, head and
20 neck cancer, melanoma, colo-rectal cancer, leukemia, endometriosis, benign prostatic hyperplasia, restenosis, atherosclerosis, rheumatoid arthritis, psoriasis, proliferative retinopathy, angiogenic retinopathy or macular degeneration.

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16. A method for treating a patient in need of increased angiogenesis comprising the step of introducing into said patient a chemical entity which causes increased expression of a functional Erk5 protein in said
30 patient.

17. The method according to claim 16, wherein said patient is characterized by reduced Erk5 activity.

18. The method according to claim 16 or 17,
5 wherein said patient is suffering from diabetic neuropathic ulcers; wounds; other ulcers, such as those of the skin and digestive organs; limb ischemia, such as fibromuscular dysplasia, thromboangitis obliterans (Buerger's disease), vasculitis, acute arterial occlusion,
10 atheroembolism, Raynaud's phenomenon or Raynaud's disease; stroke; bone fracture; periodontosis; dementia; head injury or trauma; alopecia; burns; or atherosclerosis; or is undergoing heart bypass surgery.

19. The method according to claim 18, wherein said patient is suffering from diabetic neuropathic ulcers; wounds; other ulcers, such as those of the skin and digestive organs; Raynaud's phenomenon, Raynaud's disease or alopecia.

20. The method according to any one of claims 13 to 15, further comprising the step of administering to said patient an additional therapeutic agent which is normally administered as a monotherapy to treat or prevent
25 said condition.

21. The method according to any one of claims 13 to 15, wherein said pharmaceutically acceptable composition further comprises a therapeutic agent which
30 is normally administered as a monotherapy to treat or prevent said condition.